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EDITORIAL COMMENT

New Transcatheter Aortic Valve Prosthesis Sets a New Standard*

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When Cribier et al. (1) first described transcatheter aortic valve replacement (TAVR) for aortic stenosis (AS) in 2002, few envisioned the current widespread utilization of this novel technique. Initial randomized studies provided evidence for efficacy in patients not suitable for open surgical aortic valve replacement (2,3). Subsequent studies demonstrated noninferiority (4) and then superiority (5) to surgery for high-risk patients. Nonetheless, limitations of TAVR, particularly vascular complications, stroke, and paravalvular leaks (PVL) resulting in aortic regurgitation (AR), have combined to restrict TAVR to patients with high or high-intermediate risk for surgery (6).

A breakthrough in technology or in the procedure is needed if TAVR is to continue to march down the risk profile curve. The SAPIEN 3 balloon-expandable prosthesis (Edwards Lifesciences Inc., Irvine, California) may be the spark that raises the bar for other prostheses to match and allows cardiologists and cardiothoracic surgeons to feel comfortable extending this technology to truly intermediate and low-risk surgical patients with AS.

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In this issue of the *Journal*, Webb et al. (7) report the first multicenter experience at 16 Canadian and European sites with SAPIEN 3 in 150 high- (first 50 patients) and intermediate-risk subjects with a mean age of 84 years and Society of Thoracic Surgeons (STS) predicted risk for 30-day mortality of 7.4%. This next-generation device has a balloon-expandable cobalt-chromium frame with bovine pericardial leaflets and an external fabric seal. It is one of the lowest profile devices under investigation in the United States. The use of trancatheter alternative access was surprisingly high at 36%, partly by study design. Nevertheless, the results in the transfemoral (TF) subgroup—96% fully percutaneous—were remarkable. In the 96 TF patients, the rate of all-cause mortality was 2.1% (1.1% in those with a valve implanted), all strokes 1.0%, major vascular complications 4.2%, and moderate PVL/AR 3.5%, with no patient having severe AR (7). Red flags raised by this study include the high use of alternative access with less favorable results due in part to the higher-risk profile of these subjects, a minor vascular complication rate of close to 20% even in TF patients, mild AR in 22%, and a new permanent pacemaker rate that is higher than usually seen for balloon-expandable devices at 13.3%.

What are the implications of these findings for TAVR with this device? First, transfemoral access should be the default strategy for the great majority of operators and patients. Early data with larger devices suggested equivalence and some advantages to alternative access approaches, namely fewer vascular complications and potentially fewer strokes (8). However, with smaller devices, increasing experience with femoral closure devices, monitored anesthesia care, and learning curve issues with alternative access, it has become clear that patients recover faster with percutaneous TF access and have similar or fewer complications (9), including possibly improved survival (10). In the present study, 30-day mortality was 10-fold higher (11.1%) in patients who had alternative (non-TF) access, despite similar STS risk scores. The present report does not make clear why alternative access was used so frequently nor the

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breakdown of access among high versus intermediate risk patients.

Second, the data of Webb et al. (7) create disappointment and dissatisfaction with the second-generation devices currently available. It is clear that moderate and severe AR, and in some studies mild AR, after TAVR reduces medium-term survival (11–13). Debate will continue on the methodology for assessment (12) and the rates of PVL between the commercially available devices (13), but as shown in **Table 1** comparing the largest randomized trials of TAVR devices as well as the U.S. STS/American College of Cardiology Transcatheter Valve Therapy high-risk registry, the best case scenario with TF SAPIEN 3 has set a new standard for the worst complications of TAVR, creating hunger for this and other new prostheses. In the United States, it is hoped that the results of the high- and intermediate-risk registries with this new device will reproduce these results and garner rapid U.S. Food and Drug Administration approval. In this regard, as the authors point out, while awaiting the results of the randomized PARTNER II (Placement of Aortic Transcatheter Valve) trial Cohort A (NCT01314313) and SURTAVI (Surgical Replacement and Transcatheter Aortic Valve Implantation; NCT01586910) trials in intermediate-risk patients, these data provide justification for the ongoing nonrandomized SAPIEN 3 intermediate-risk cohort registry of the PARTNER II trial.

One can now envision that this and other third-generation TAVR devices will move this procedure into low intermediate- and truly low-risk patients.

TABLE 1 30-Day Outcomes in Selected TAVR Trials

Trial (Ref. #)	N	STS Score	Mortality	All Stroke	≥ Moderate AR	Major Vascular Complications	New PPM
PARTNER IB (2)	179	11.2	5.0	6.7	11.8	16.2	3.4
PARTNER IA (4)	348	11.8	3.4	4.7	12.2	11.0	3.8
PARTNER IIB (14)	284	10.3	3.5	4.3	24.0	9.6	6.4
STS/ACC TVT registry (6)	3,528	7.0	7.6	2.8	–	–	6.6
CoreValve extreme (3)	489	10.3	8.4	4.0	15.3	8.2	21.6
CoreValve pivotal (4)	390	7.3	3.3	4.9	10.0	5.9	19.8
SAPIEN 3 (7)	150	7.4	5.3	2.7	3.5	5.3	13.3
SAPIEN 3 TF cohort (7)	96	7.5	2.1	1.0	3.5	4.2	12.5

Values are % unless otherwise indicated.

ACC = American College of Cardiology; AR = aortic regurgitation; PARTNER = Placement of Aortic Transcatheter Valve; PPM = new permanent pacemaker; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement; TF = transfemoral; TVT = transcatheter valve therapy.

TAVR may then become the treatment of choice for the majority of patients with severe and symptomatic AS. However, the excitement that this new device provides to the TAVR community should be tempered by the lack of data on long-term durability, a permanent pacemaker rate higher than observed with previous balloon-expandable valves, and the residual mild AR rate. Nonetheless, the bar has been raised and a new standard for TAVR results has been set.

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